

JC20 Rec'd PCT/PTO 20 JUN 2005

Claims

1. A nucleic acid molecule encoding an inactive form of the human transcription initiation factor TIF-IA, wherein said human transcription initiation factor TIF-IA is not or not completely posttranslationally modified.

2. The nucleic acid molecule of claim 1, wherein the serine residue at position 633 and/or 649 is replaced by another amino acid residue.

3. The nucleic acid molecule of claim 2, wherein the serine residue at position 649 is replaced by an alanine residue.

4. The nucleic acid molecule of claim 1, wherein at least one amino acid residue being part of the recognition motif for a phosphatase or kinase comprising the serine residue at position 633 and/or 649 is replaced by another amino acid residue.

5. The nucleic acid molecule of claim 1, wherein the serine residue at position 44 and/or 199 is replaced by another amino acid residue.

6. The nucleic acid molecule of claim 5, wherein the serine residue at position 44 is replaced by an alanine residue or an aspartic acid residue and/or the serine residue at position 199 is replaced by an aspartic acid residue.

7. The nucleic acid molecule of claim 1, wherein at least one amino acid residue being part of the recognition motif for a phosphatase or kinase comprising the serine residue at position 44 and/or 199 is replaced by another amino acid residue.

8. A recombinant vector containing the nucleic acid molecule of any one of claims 1 to 7.

9. The recombinant vector of claim 7 wherein the nucleic acid molecule is operatively linked to regulatory elements allowing transcription and synthesis of a translatable RNA in prokaryotic and/or eukaryotic host cells.

10. The recombinant vector of claim 8 or 9 which is a vaccinia based expression vector.

11. A recombinant host cell which contains the recombinant vector of any one of claims 8 to 10.

12. The recombinant host cell of claim 11, which is a mammalian cell, a bacterial cell, an insect cell or a yeast cell.

13. An inactive human transcription initiation factor TIF-IA which is encoded by a nucleic acid molecule of any one of claims 1 to 7.

14. A method of producing an inactive human transcription initiation factor TIF-IA comprising:

- (a) culturing the recombinant host cell of claim 11 or 12 under conditions such that said TIF-IA is expressed; and
- (b) recovering said TIF-IA.

15. An inactive human transcription initiation factor TIF-IA produced by the method of claim 14.

16. A transgenic non-human animal comprising at least one nucleic acid molecule of any one of claims 1 to 7 or the recombinant vector of any one of claims 8 to 10.

17. A cell line comprising at least one nucleic acid molecule of any one of claims 1 to 7 or the recombinant vector of any one of claims 8 to 10.

18. The transgenic non-human animal of claim 16 or the cell line of claim 17 further comprising at least one wild type allele of the TIF-IA encoding gene.

19. The transgenic non-human animal of claim 16 or 18 which is a mouse or rat.

20. A pharmaceutical composition comprising a nucleic acid molecule of any one of claims 1 to 7, a TIF-IA polypeptide of claim 13 or 15, or a recombinant vector of any one of claims 8 to 10 and a pharmaceutically acceptable excipient, diluent or carrier.

21. A method for identifying compounds capable of inhibiting the conversion of an inactive pre-form of TIF-IA into a biologically active form, said method comprising the steps of:

- (a) contacting a cell which expresses TIF-IA and all factors required for said conversion of said TIF-IA with a compound to be screened; and
- (b) determining if the compound inhibits the conversion of an inactive pre-form of TIF-IA into a biologically active form.

22. Use of a nucleic acid molecule of any one of claims 1 to 7, a TIF-IA polypeptide of claim 13 or 15, or a recombinant vector of any one of claims 8 to 10 for the preparation of a medicament for treatment of a disease which is associated with an increased cell proliferation.

23. Use according to claim 22, wherein the disease is a tumor.